

IN THE SPECIFICATION:

Please replace the title at page 1, line 1, with the following title:

**PROBE COMPOSITION AND METHOD METHOD FOR DISTINGUISHING
DIFFERENT-SEQUENCE POLYNUCLEOTIDES**

Please replace the paragraph at page 1, lines 4 to 14 (the original paragraph at page 1, lines 4 to 14 was replaced with a replacement paragraph in the Preliminary Amendment filed April 14, 2004) with the following paragraph:

This is a continuation of U.S. Application No. 10/167,337 filed June 10, 2002, now U.S. Patent No. 6,759,202, which is a continuation of U.S. Application No. 09/580,680 filed May 30, 2000, which is a continuation of U.S. Application No. 09/111,632 filed July 7, 1998, now abandoned, which is a continuation of U.S. Application No. 08/643,709 filed May 6, 1996, now Pat. No. 5,777,096, which is a continuation of U.S. Application No. 08/102,372 filed August 4, 1993, now Pat. No. 5,514,543, which is a continuation-in-part of U.S. Application No. 07/973,118 filed November 6, 1992, abandoned, which is a continuation-in-part of U.S. Application No. 07/866,018 filed April 7, 1992, now Pat. No. 5,470,705 which is a continuation-in-part of U.S. Application No. 07/862,642 filed April 3, 1992, abandoned, all of which are incorporated herein by reference.

Please replace the paragraph beginning on page 55, line 2, and ending on page 55, line 11, with the following paragraph:

A 48-base oligonucleotide having the sequence
5'GCACCATTAAGAAAATATCATCTTTGGTGTTCCTATGATGAATATA
carboxyfluorescein-3' (SEQ ID NO: 1) (composition 10 in Figure 4A) was prepared
using a 3'-linked carboxyfluorescein polystyrene support (Applied Biosystems, Inc.) or
can be prepared using 3'-Amine-ON CPG (Clontech, Palo Alto, CA) and FAM-NHS
(ABI) according to published methods (Applied Biosystems, Caruthers, Connell) and
standard phosphoramidite chemistry on an Applied Biosystems 380B DNA Synthesizer.

Please replace the paragraph beginning on page 56, line 18, and ending on page
56, line 27, with the following paragraph:

A 26 base oligonucleotide having the sequence 5' TTG GTG TTT CCT ATG ATG
AAT ATA-LAN-T3' (SEQ ID NO: 2) was made on an ABI model 380B DNA synthesizer
using standard phosphoramidite chemistry (composition 15 in Figure 5). LAN is a base-
modified deoxyuridine phosphoramidite (Molecular Biosystems Inc.) with a TFA-
protected amine. The 26-mer was made from a 1 μ mol column using trityl on manual
protocol after completion of synthesis. The column material was divided into 10
separate 0.1 μ mol columns.

Please replace the paragraph beginning on page 57, line 27, and ending on page
57, line 31, with the following paragraph:

A 25 base oligonucleotide having the sequence 5' GGC ACC ATT AAA GAA
AAT ATC ATC T 3' (SEQ ID NO: 3) was made as described in Example 4A. DMT-

protected phosphoramidite HEO units were added to the 5' end of this 25 mer and purified as described in Example 4B.

Please replace the paragraph beginning on page 58, line 4, and ending on page 58, line 16, with the following paragraph:

A 25-mer oligonucleotide having the sequence 5' GGC ACC ATT AAA GAA AAT ATC ATC T 3' (SEQ ID NO: 3) was prepared and de-tritylated on a CPG support as described above. The 5' -hydroxyl group of the 25-mer was then derivatized with N-MMT-C₆ Amino Modifier (Clontech Laboratories, Palo Alto, CA; Compound 20 in Fig. 6) using standard phosphoramidite chemistry. The monomethoxytrityl group was removed using a standard trityl cleavage protocol on an ABI DNA synthesizer (yielding Compound 21 in Fig. 6.), and the DNA synthesis column was then transferred to an ABI Peptide synthesizer capable of performing Fmoc chemistry.

Please replace the paragraph beginning on page 60, line 29, and ending on page 61, line 4, with the following paragraph:

The synthesis column was then placed onto an ABI DNA synthesizer and the peptide-oligonucleotide was cleaved off the support and purified by HPLC using the conditions as previously described to produce the peptide-oligonucleotides Ac-(Phe-Ala)_{2 or 4}-NH(CH₂)₆-phosphate 5' GGC ACC ATT AAA GAA-AAT ATC ATC T-3' (SEQ ID NO: 3). Ligation of the peptide-oligonucleotide to a fluorescent-labeled oligonucleotide in the presence of an oligonucleotide target was performed as described in Example 8.

Please replace the paragraph beginning on page 61, line 8, and ending on page 61, line 18, with the following paragraph:

A first probe having the sequence 5' GGC ACC ATT AAA GAA AAT ATC ATC T-3' (SEQ ID NO: 3) was derivatized with [[a]] either a tetrapeptide Phe-Ala-Phe-Ala (SEQ ID NO: 4) or an octapeptide Phe-Ala-Phe-Ala-Phe-Ala-Phe-Ala (SEQ ID NO: 5) according to methods in Example 7. A second probe having the sequence 5' P-TTG GTG TTT CCT ATG ATG AAT ATA G JOE 3' (SEQ ID NO: 6) was prepared with 3-amine-ON CPG, and 5'-phosphate-ON, both from Clontech (Palo Alto, CA), and with JOE-NHS (Applied Biosystems, Inc.) using published methods (Applied Biosystems Bulletin; Aruthers; Connell).

Please replace the paragraph beginning on page 62, line 6, and ending on page 62, line 20, with the following paragraph:

The following four probes were prepared:

- (1) 5' GGC ACC ATT AAA GAA AAT ATC ATC T-3' (SEQ ID NO: 3) derivatized at its 5' end with [[a]] either a 2 or 4 unit DEO (dodeca-(ethylene oxide)) polymer chains, according to synthetic methods described in Example 4, except in this case the units are 12-mers (2 or 4 12-mers) of ethylene oxide;
- (2) 5' P-TTG GTG TTT CCT ATG ATG AAT ATA G 3'-JOE (SEQ ID NO: 6), prepared as in Example 8;
- (3) 5' ROX-CTA TAT TCA TCA TAG GAA ACA CCA AA 3'-OH (SEQ ID NO: 7), prepared according to published methods (Applied Biosystems);
- and (4) 5'-P-GAT GAT ATT TTC TTT AAT GGT GCC-3' TAMRA (SEQ ID NO: 8),

prepared with 3'-Amine-ON CPG, 5'-Phosphate-ON and Tamra-NHS (ABI) using published methods (Applied Biosystems, Caruthers, Connell).

Please insert the enclosed sequence listing starting on a new page immediately following the abstract on page 75.